REMARKS

The claims have been amended to correct typographical errors. The claims have also been amended in response to the Examiner's rejections under 35 USC 112, second paragraph as discussed below. Additionally, amendments have been proposed in claim 30, which further limit the scope of the invention and to further clarify the differences between the present invention and the prior art. Previously submitted dependent claim 55 is also being incorporated into independent claim 30. Basis for these amendments can be found in the specification in the paragraphs joining pages 11 and 12 and pages 13 and 14. These amendments have been proposed so that one may have a better understating of the "use" of electrically conducting material" and "magnetic material". These limitations also satisfy the Examiner's observation that the claims have not been directed to "a method of detecting the contraceptive" [joining paragraph of pages 7-8 of the Office Action] and "a method of removing the contraceptive" [second paragraph of page 8 of the Office Action] and to clarify that these ingredients have been incorporated for novel and inventive use, and not for the known use.

In this office action the Examiner rejected claims 32, 36, 47-54 and 56 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is indefinite because it is unclear if the iron is meant to be selected from iron oxide and iron in a composition with a biologically accepted material and if so, it is unclear whether or not the iron is the composition needs to be iron oxide. Further, it is unclear what Applicant means by "like sulfur". Is the biological material "like" sulfur, or is it a material "such as" sulfur? If a material is "like" sulfur, does that mean that sulfur is excluded from the scope of the claim? Furthermore, how closely related to sulfur must the material be to be "like" sulfur?

Applicant has **amended claim 32** to clarify that magnetic material is iron in its pure form or in the form of its oxide or in a combination with a biologically accepted material, such as sulfur. The word "like" has been replaced with "such as".

Claim 36 is indefinite because there are no units for the upper limit of the range of the size of the macrosize particles.

Applicant has **amended claim 36** and provided the units for the upper limit of the range of the size of the macrosize particles.

Claim 47 is indefinite because neither the claim nor the claims from which it depends mention anything about an external means or the purpose of said external means. Does Applicant intend to say that the contraceptive is detectable by the external means listed in the claim?

Applicant respectfully submits that the dependency clause of **claim 47** has been **amended** to have dependency from preceding claim 46 and confirms that this claim defines "external means" which

include ultrasound, X-ray, CAT scan, MRI **and** scanning electrical impedance plethysmography. Applicant also submits that claim 46 from which claim 47 depends defines the purpose of said external means as "to detect the presence of the contraceptive from outside the body", which is carried out by the external means defined in **claim 47**.

Applicant confirms that the contraceptive is detectable by **all** the external means listed in claim 47.

Claim 48 is rejected being indefinite because there is lack of antecedent basis for "said magnetic material" and "said solvent medium".

Applicant has **amended claim 48** by replacing the word "said" with "a" appropriately.

Claims 49-54 and 56 are rejected for depending from indefinite claims.

As amended **claim 48**, from which these claims depend, has been amended, this rejection may please be reconsidered and withdrawn.

Arguments

Claims 30-47 and 50 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Guha (USPN 5,488,075) in view of each of Young et. Al. (USPN 5,817,017), Riar, et al. (Andrologia, 1982, 14(6), 481), and Jakubek, et. Al. (GB 2,112,289A).

The Learned Examiner is of the opinion that Guha teaches the use of a styrene maleic anhydride copolymer with DMSO as a contraceptive (col. 1, lines 54-62). It further teaches that when

injected into the vas deferens, the contraceptive copolymer **hydrolyzes** in the presence of water molecules in the spermatic fluid (col. 2, lines 45-col. 3, line 7). Accordingly, it is **Examiner's interpretation**, that Guha teaches a composition comprising DMSO and a mixture of styrene maleic anhydride copolymer and the hydrolyzed copolymer thereof, namely styrene maleic acid copolymer.

The Learned Examiner states that **"absent a showing to the contrary**, it is the Examiner's position that the hydrolysis of styrene maleic anhydride, as taught by Guha, **would necessarily**, produce styrene maleic acid.

Applicant respectfully submits that Guha **neither teaches nor even indicates** that the "hydrolysis of styrene maleic anhydride would necessarily produce styrene maleic acid". **On the contrary**, Guha only teaches and clearly indicates that "styrene maleic anhydride (the contraceptive copolymer as per Guha) hydrolyzes in the presence of water molecules in the spermatic fluid. **The polymer has cyclic group which breaks upon hydrolysis and the anhydride is converted to a hydride**. Due to such a conversion of anhydride to hydride, the polymer develops a positive charge, which disturbs the negative charge of the sperm membrane" [Col. 2, Lines 54-61]. Accordingly, the Learned Examiner's position that Guha teaches that "styrene maleic anhydride on hydrolysis would necessarily produce styrene maleic acid" is not persuasive.

Further, it is submitted that according to Guha, styrene maleic anhydride [SMA] forms a complex SMA-DMSO with DMSO, which reacts with amino acids to detach DMSO from SMA while retaining the broken bond and consequent polyelectrolyte structure of the SMA. Thus, the COOH of the maleic anhydride exists as COO^-+^+H. The place of DMSO is taken over by the proteins of the spermatic fluid with polar amino acids of the proteins linked to the SMA and sustaining the polyelectrolyte nature induced into the SMA. That is, the negative charge of COO^- and the positive charge of H^+ are maintained in a bound state. The proteins form a layer around the SMA [Col. 3, Lines 62 - Col 4, Lines 23]. It has been observed that protein layer over the SMA gives a protection to the SMA from dissolution. This phenomenon gives the long-term action of the contraceptive in the vas deferens [Col 4, Lines 35-38].

Accordingly, it is clear that Guha neither teaches nor even indicates that styrene maleic anhydride hydrolyzes to styrene maleic acid on injection in the lumen of vas deferens or of fallopian tube **to necessarily produce styrene maleic acid copolymer to result in** the claimed composition ***in vivo*** comprising mixture of styrene maleic anhydride and styrene maleic acid, that is based on Guha either alone or in combination with Young et al., Riar, et al., and Jakubek, et al. it **cannot be held** that addition of an iron material and a copper material to the styrene maleic anhydride composition of Guha **would have necessarily produced** the claimed composition *in vivo* because Guha teaches that hydrolysis of the

styrene maleic anhydride copolymer is known to occur once injected to produce styrene maleic acid copolymer. Applicant agrees that hydrolysis of styrene maleic anhydride is known to occur, but this hydrolysis, according to Guha et al., **does not produce styrene maleic acid. On the contrary**, according to Guha et al. styrene maleic anhydride on hydrolysis produces hydride [Col. 2, Lines 54-61] or on reaction with amino acids produces polyelectrolyte structure of SMA [Col 3, Lines 62 - Col. 4, Lines 8]. Accordingly, the reading of Guha neither teaches nor even indicates to the person of the ordinary skill to combine styrene maleic anhydride copolymer with styrene maleic acid copolymer to arrive at the claimed composition.

In view of above submissions, one cannot obviously conclude that on combined readings of Young et al., Riar et al., and Jakubek et al. with teachings of Guha one will obviously arrive at the claimed composition comprising a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer in the selected ratio.

Further, the ***in vivo* hydrolysis** of styrene maleic anhydride cannot be compared with or considered equivalent to ***in vitro* hydrolysis**, because the former process is uncontrolled process and dependents on subject's physiological conditions, and hence, the amount of styrene maleic anhydride vis-à-vis styrene maleic acid cannot be controlled. **On the contrary**, in the present invention the relative ratio of styrene maleic anhydride copolymer and styrene

maleic acid copolymer can be controlled to the selected level as it is not dependent upon subject's physiological condition. The conversion of styrene maleic anhydride to styrene maleic acid, **if at all it is taking place as opinioned by the Learned Examiner contrary to the teachings of Guha** *may* continue and *may* result in formation of styrene maleic acid which being soluble in water will wash out and the contraceptive effect will be reduced to few days **contrary** to findings of clinical trials of contraceptive formulation taught by Guha which have proved that it has contraceptive effect of longer duration [Col 4, Lines 35-38].

Further, the *in vitro* results **cannot be compared** with *in vivo* results, that is if a substance on *in vitro* hydrolysis results in a particular substance, then it **cannot be obviously concluded** that the said substance will obviously result in same particular substance *in vivo*. Had this theory been true, then all substances which have proved during the *in vitro* studies should have shown same results during the *in vivo* studies, that is there was no need to conduct *in vivo* studies once the results of *in vitro* studies have proved to be acceptable. The acceptance of this theory would mean that a pharmaceutical substance or a pharmaceutical composition or a pharmaceutical formulation can be introduced for the use of human beings if its *in vitro* studies show acceptable results. It is well established that this is not the actual state of affair. **On the contrary**, each and every substance is subjected to *in vivo* studies after acceptable results of *in vitro* studies,

and it has been found that in majority of cases, the results during the *in vivo* studies are contrary to the results during the *in vitro* studies.

Applicant respectfully also submits that Guha was also cited in the ISR, but under "A" category and corresponding European patent application has been accepted, a copy of notification from the European Patent Office (EPO) along with set of accepted claims are enclosed for ready reference of the Learned Examiner. The allowance of corresponding European patent application also confirms Applicant's opinion about Guha et al. and other cited documents.

Now, as it has been established and held that Guha neither teaches nor even indicates that styrene maleic anhydride hydrolyzes to styrene maleic acid to produce a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer of the claimed composition, Learned Examiner's rejection of claimed composition based on combined reading of Guha et al., Young et al., Riar et al., and Jakubek et al. is not sustainable.

The Learned Examiner is of the opinion that "use of magnetic particles such as iron, including elemental iron and iron oxides for enhanced detectability by MRI" is taught by Young et al. The Learned Examiner has rejected Applicant's submission that Young et al. limits the use of iron particles in the catheters or conventional devices only for MRI **because Applicant's claims** are not directed to "a method of detecting the contraceptive, but to

the contraceptive composition itself". Furthermore, the Learned Examiner notes that none of Applicant's claims indicate that the material **must** be detectable by ***all*** recited means. Finally, he notes that since the addition of the magnetic material would have been obvious for the reasons stated above, the same composition will, obviously, have the same properties as the composition claimed.

Applicant confirms that claim 46 provides that the presence of the contraceptive is **detected by imaging** from outside the body by external means, and **claim 47**, now dependent on preceding claim 46 defines said **external means** including ultrasound, X-ray, CAT scan, MRI **and** scanning electrical impedance plethysmography [page 1, lines 10-11; page 10, lines 25-29; page 11, lines 29-33 and page 12, lines 1-3 of the PCT publication]. The presence of present contraceptive formulation is detectable due to mechanical characteristic impedance to the passage of ultrasound becoming significantly different from that of body tissue and hence the **presence** of the contraceptive within the body and its **location** can be determined by ultrasonography **[page 11, lines 29-33]**. The present invention also visualizes, the **determination of the quantum** of present contraceptive formulation by magnetic field estimations **as well as** by X-Ray imaging, CAT scan, MRI scan **and** scanning electrical impedance plethysmography **[joining paragraph of pages 11 and 12; page 13, lines 9-14]**. Furthermore, in accordance with the present invention, the **fertility can be restored**, that is

contraceptive formulation can be **removed** from the vas deferens or fallopian tube, as and when desired by the subject by using the magnetic properties of the present contraceptive formulation to propel the contraceptive for voiding and restoration of fertility by external magnetic field **[page 12, Lines 25-28]** which is neither taught nor indicated in Young et al.

Accordingly, the persons with ordinary skill in the art will not obviously incorporate the magnetic particles after reading of Young et al. for achieving the **capability of imaging or detecting the presence and location of the contraceptive by external means including** X-Ray imaging, CAT scan, MRI scan **and** scanning electrical impedance plethysmography, **and as well as for partly quantifying the contraceptive present in the lumen of vas deferens or fallopian tube** by measuring the residual magnetic field strength from outside the body, and for restoration of the **fertility of the subject**, that is removal of the contraceptive formulation from the vas deferens or fallopian tube.

The Learned Examiner indicates that the claims are not directed to "a method of detecting the contraceptive", but to the contraceptive composition itself. Applicant has amended present **claim 30** to restrict its scope by way of defining the "use of magnetic particles" therein.

Applicant also confirms that **claims 46 and 47** confirm that the contraceptive material **is** detectable by ***all*** recited means. The word

"**and**" in **claim 47** and in page 1, lines 10-11; page 10, lines 25-29; page 11, lines 29-33 and page 12, lines 1-3 of the PCT publication clearly confirms this submission.

Accordingly, the addition of magnetic material would not been obvious for the purposes of "*in vivo* quantification of contraceptive", "*in vivo* control of flow of contraceptive" and "reversal of contraceptive" and it obviously would not have resulted in the claimed composition having said properties which are entirely different from the properties of the formulation taught by Young et al. Accordingly, it is clear from the **amended claim 30** that the present invention teaches contraceptive formulation having distinct properties than the formulation taught in the prior art.

Therefore, in view of above submission and **amended claim 30**, it cannot be held that Young et al. obviously teaches the present contraceptive formulation having defined capabilities / properties.

The Learned Examiner is of the opinion that Riar et al. teaches that **copper deposited into vas deferens** of animals is effective at achieving a male contraception for **9 months**. The Learned Examiner states that it would have been obvious to add copper to the composition for contraceptive effect. The Learned Examiner also notes that claims are not directed to "a method of removing the contraceptive", but to the "contraceptive composition itself".

Applicant respectfully submits that when copper is used in the

manner as taught by Riar et al. it only results in the contraceptive effect up to 9 **months. On the contrary,** the contraceptive effect of the claimed composition has been observed, **by subsequent studies, to be up to 10 years.** This is due to the reason that Riar et al. employs and uses copper for its chemical properties. **On the contrary,** the presently claimed composition shows contraceptive effect due to the selected mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, which happens due to the swelling and anchoring properties of the claimed contraceptive copolymer mixture without adhesion **[Page 12, Lines 14-16].** Further, presently claimed composition employs copper for its electrical and electrically conducting properties to restore the fertility, that is to remove the contraceptive from the reproductive tract, as and when desired by the subject. The removal of contraceptive is achieved by heating the claimed contraceptive formulation by virtue of its electrical properties by electromagnetic induction with fields from outside the body. The heating changes the basic polymer characteristics thereby lowering its contraceptive action to obtain restoration of fertility as and when desired. The removal of contraceptive is further facilitated by lowering of viscosity of the contraceptive on induction heating which further facilitates its removal from the body by an externally imposed magnetic field, preferably traveling magnetic field so as to restore reproductive functions as and when desired **[Page 12, Lines 4-13]. Such surprising effects of combining**

electrically conducting material - copper with copolymer composition of present invention and combining magnetic material - iron in its pure form or in the form of oxide or in the form of combination with biologically acceptable material were neither taught nor even indicated by Riar et al. and/or by Young et al. Accordingly, it cannot be held that it would have been obvious for the persons of ordinary skill in the art to combine copper and iron with copolymer of Guha to arrive at the presently claimed composition.

Applicant confirms that it is now clear that neither copper nor iron are employed for their **very known purposes**, that is for short term contraceptive action and imaging respectively, but are employed for their explained **surprising effects** for restoration of fertility, that is for the enhanced capability for **removal** of contraceptive as and when desired by the subject, and for ***in vivo* quantification** of the contraceptive and ***in vivo* control** of distribution of the contraceptive. These features have been claimed in **claims 43 to 47.**

Applicant has now **amended claim 30** to clarify the above properties and surprising effects of copper and iron in the claimed composition. However, as desired by the Learned Examiner, in view of above submissions claims on file **may not be required** to be directed to "a method of detecting the contraceptive ... ..." or "a method of removing the contraceptive .....", because the

contraceptive formulation *per se* is not only novel, but also involves an inventive step which cannot be obvious from the reading of one or more of the cited documents.

The Learned Examiner is of the opinion that Jakubek et al. teaches the use of a polymer mixed with 1 to 30% by weight of a powder metal, such as copper, **as a contraceptive, that is for contraceptive use**. The powdered metal is distributed throughout the polymer material and has a particle size of 2 to 50 μm. The Learned Examiner has also opinioned that one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of reference. The Learned Examiner has also opinioned that if the prior art **structure is capable of performing the intended use for contraceptive uses by injecting into the vas deference**, then it meets the claims.

Applicant respectfully submits that Learned Examiner's opinion is based on abstract of Jakubek et al. However, from the reading of the specification of Jakubek et al. one will observe that **primary purpose of combining copper** with polymer is to have an IUCD whose shape and size approaches the shape and size of the uterine cavity into which the IUCD shall be inserted as optimally as possible, that is to have **sufficient resilience to adjust to changes** in the shape of uterine cavity during menstrual cycles and during uterine contractions. Jakubek et al. proposes that the device should have **sufficient plastic shape memory** to return to its original shape and original position, and to overcome problems of bleeding, expulsion

and pain in the uterine cavity **[Page 1, Lines 1-60]**. It has been observed by Jakubek et al. that increasing amounts of metal results in greater likelihood of IUCD retaining its resilience **[Page 2, Lines 9-11]**. It has been stated in Jakubek et al. that the **contraceptive effect is complex and caused by stimulation of natural defensive capabilities of human body**. According to Jakubek et al., the metal, copper is **released continuously** throughout uterine cavity **[Page 2, Lines 66-72]**. The metal gets to surface of device, and diffuses from interior of device to its surface. The speed of release of metal from polymer material is influenced by swelling of IUCD.

On the contrary, in the claimed contraceptive composition, as stated hereinabove, copper is **neither** employed *merely* for contraceptive use **nor** for enhancing the resilience property of polymer or device, but for its **electrical properties** which have shown surprising effects for restoring the fertility by removing the contraceptive formulation. Accordingly, it cannot be held that combination of copper with a polymer is for vary same purpose in Jakubek et al. and/or in Riar et al. when compared with present invention. It may be noted that even the method of preparing the polymer combined with copper is entirely different in Jakubek et al. and present invention resulting in structural changes.

Applicant further submits that the **intended purpose** of present invention is not only to have a **contraceptive formulation *merely***

for contraceptive use, but to have a contraceptive formulation having capability of *reversal by external means* in non-invasive manner to have fertility as and when desired, and the capabilities of *in vivo quantification* and *in vivo control of flow* of the contraceptive formulation in-addition to having contraceptive effect, which means that by reading of Jakubek et al. with other cited documents, one cannot obviously arrive at the claimed composition.

It is now also clear from above submissions that the claimed contraceptive formulation is **structurally distinct** from the formulations of the cited documents as it comprises ***i)*** a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer to have contraceptive effect, and ***ii)*** an electrically conducting material having charge transfer, sperm membrane and ovum covering molecule exchange, and inductive heating properties *for the purpose* of restoring the fertility by removing the contraceptive and ***iii)*** a magnetic material having magnetizing and magnetic force drag properties *for the purpose* of *in vivo* detection, *in vivo* quantification, *in vivo* control of flow and enhanced reversal of contraceptive as and when desired in ***iv)*** a solvent medium, [page 11, lines 25-29; page 12, lines 22-24; page 13, lines 2-3 and 27-29; and line 33 of page 13 to line 3 of page 14 read with page 18, lines 13-26 and page 19, lines 9-15 of PCT publication], and such combination is neither taught nor indicated

by one or all the cited documents. Accordingly, the claimed composition is not obvious by the cited prior art for performing the intended use. Even the selection of selected amounts of the selected materials cannot be considered as *merely* being a discovery of optimum value of a result effective variable.

Conclusion

In view of above submissions and enclosed further amended claims, Applicant respectfully requests that the Learned Examiner enter the above amendment and withdraw his rejections of claims under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention, and under 35 U.S.C. 103(a) as being unpatentable over Guha (USPN 5488075) in view of each of Young et al. (USPN 5817017), Riar, et al. (Andrologia, 1982, 14(6),481). and Jakubek, et al. (GB 2 121 289 A).

In view of the amendment to the claims and the discussion supra it is believed that claims 30-47 and 55 are patentable. Therefore, Applicant believes that this application is now in condition for allowance and such allowance by the Examiner is respectfully requested.

If entrance of this amendment is denied and/or if the Examiner believes that entrance of this amendment does not place this application in condition for allowance, then he/she is requested to contact the undersigned Agent for Applicant by telephone at

(412)380-0725 to discuss possible alternative claim language.

In the event the Learned Examiner has further difficulties with the examination and/or allowance of the application, the Learned Examiner is invited to contact the undersigned Agent for Applicant by telephone at (412) 380-0725, if necessary, to resolve any remaining questions or issues by interview and/or Examiner's Amendment as to any matter.

Respectfully submitted,

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